

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
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Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 March 1999 (22.03.99)	
International application No. PCT/EP98/04945	Applicant's or agent's file reference T/97300 WO
International filing date (day/month/year) 05 August 1998 (05.08.98)	Priority date (day/month/year) 08 August 1997 (08.08.97)
Applicant GOUDSMIT, Jaap et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
08 February 1999 (08.02.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Dominique DELMAS

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 07 SEP 1999

WIPO PCT

Applicant's or agent's file reference T/97300 WO	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP98/04945	International filing date (day/month/year) 05/08/1998	Priority date (day/month/year) 08/08/1997	
International Patent Classification (IPC) or national classification and IPC C12Q1/70			
Applicant AKZO NOBEL N.V. et al.			


1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 08/02/1999	Date of completion of this report 02.09.99
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hinchliffe, P Telephone No. +49 89 2399 8431



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP98/04945

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-22 as originally filed

Claims, No.:

1-10 as received on 25/08/1999 with letter of 20/08/1999

Drawings, sheets:

1/1 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP98/04945

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	10
Inventive step (IS)	Yes:	Claims	1-9
	No:	Claims	10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

SECTION V

1. The subject matter of claims 1-9 fulfills the requirements of Articles 33(2) and 33(3) PCT. Although the documents cited in the I.S.R. do provide probes which overlap in sequence with those claimed none of the documents suggests the exact primer pairs claimed for use in a PCR HIV-1 detection method. The claims thus encompass novel subject matter because this is the first time a particular combination of primers is suggested. Furthermore the choices made do appear to provide a better detection of HIV infection over those disclosed in the prior art methods (see example 4). As the particular choices of primer result in improved detection, the subject matter of the claims also appears to involve an inventive step.
2. However, in contrast to the above, the subject matter of claim 10 neither discloses a particular choice of primer nor any particular sequence. Consequently the said subject matter does not fulfill the requirements of Articles 33(2) or 33(3) PCT because D1-D3 disclose primer pairs which encompass locations within the LTR.

SECTION VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D3 are not mentioned in the description, nor are these documents identified therein.

CLAIMS:

1. An oligonucleotide substantially complementary to a sequence of the LTR region of a nucleic acid sequence of a HIV genome, said oligonucleotide being 10-50 nucleotides in length and comprising, at least a fragment of 10 nucleotides, of a sequence selected from the group consisting of:

SEQ ID 1: G GGC GCC ACT GCT AGA GA

SEQ ID 2: G TTC GGG CGC CAC TGC TAG A

SEQ ID 3: CGGGCGCCACTGCTA

SEQ ID 4: CTG CTT AAA GCC TCA ATA AA

SEQ ID 5: CTC AAT AAA GCT TGC CTT GA

SEQ ID 12: GAT GCA TGC TCA ATA AAG CTT GCC TTG AGT

SEQ ID 6: TCT GGT AAC TAG AGA TCC CTC

SEQ ID 7: TAG TGT GTG CCC GTC TGT

SEQ ID 8: AGT GTG TGC CCG TCT GTT

or the complementary sequence thereof.

2. An oligonucleotide according to claim 1, consisting essentially of a sequence selected from the group consisting of:

SEQ ID 1: G GGC GCC ACT GCT AGA GA

SEQ ID 2: G TTC GGG CGC CAC TGC TAG A

SEQ ID 3: CGGGCGCCACTGCTA

SEQ ID 4: CTG CTT AAA GCC TCA ATA AA

SEQ ID 5: CTC AAT AAA GCT TGC CTT GA

SEQ ID 12: GAT GCA TGC TCA ATA AAG CTT GCC TTG AGT

SEQ ID 6: TCT GGT AAC TAG AGA TCC CTC

SEQ ID 7: TAG TGT GTG CCC GTC TGT.

SEQ ID 8: AGT GTG TGC CCG TCT GTT.

SEQ ID 9: aat tct aat acg act cac tat agg gAG AGG GGC GCC ACT GCT AGA GA

SEQ ID 10: aat tct aat acg act cac tat agg gAG AGG TTC GGG CGC CAC TGC TAG A

SEQ ID 11: aat tct aat acg act cac tat agg gCGGGCGCCACTGCTA

3. Use of an oligonucleotide according to claim 1 or 2 in a nucleic acid amplification reaction or as a probe for the detection of HIV nucleic acid in a sample.

4. Pair of oligonucleotides, for use as a set in the amplification of a target sequence located within the LTR region of the genome of HIV-1, said pair consisting of a first oligonucleotide being 10-50 nucleotides in length and comprising, at least a fragment of 10 nucleotides, of a sequence selected from the group consisting of:

- 5 SEQ ID 1: G GGC GCC ACT GCT AGA GA
SEQ ID 2: G TTC GGG CGC CAC TGC TAG A
SEQ ID 3: CGGGCGCCACTGCTA

and a second oligonucleotide being 10-50 nucleotides in length and comprising, at least a fragment of 10 nucleotides, of a sequence selected from the group consisting of:

- 10 SEQ ID 4: CTG CTT AAA GCC TCA ATA AA
SEQ ID 5: CTC AAT AAA GCT TGC CTT GA.
SEQ ID 12: GAT GCA TGC TCA ATA AAG CTT GCC TTG AGT

5. Pair of oligonucleotides according to claim 3, consisting of

- 15 a first oligonucleotide being 10-50 nucleotides in length and comprising, at least a fragment of 10 nucleotides of the sequence

SEQ ID 1: G GGC GCC ACT GCT AGA GA and a second oligonucleotide being 10-50 nucleotides in length and comprising, at least a fragment of 10 nucleotides of the sequence
SEQ ID 5: CTC AAT AAA GCT TGC CTT GA.

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6. Pair of oligonucleotides according to any of claims 4-5 wherein the first oligonucleotide is provided with a promoter sequence recognized by a DNA dependent RNA polymerase.

- 25 7. Pair of oligonucleotides according to claim 6 consisting of a first oligonucleotide consisting essentially of the sequence

SEQ ID 9: *aat tct aat acg act cac tat agg g*AGG GGC GCC ACT GCT AGA GA and a second oligonucleotide consisting essentially of the sequence
SEQ ID 5: CTC AAT AAA GCT TGC CTT GA.

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8. Oligonucleotide according to claim 1, consisting essentially of the sequence

SEQ ID 6: TCT GGT AAC TAG AGA TCC CTC
SEQ ID 7: TAG TGT GTG CCC GTC TGT or
SEQ ID 8: AGT GTG TGC CCG TCT GTT

- 35 provided with a detectable label.

9. Method for the detection of HIV-1 nucleic acid in a sample wherein the sample is subjected to a nucleic acid amplification reaction using a pair of oligonucleotides according to claim 4 and suitable amplification reagents and the presence of any amplified nucleic acid is detected.

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10. Method according to claim 9, wherein the detection of any amplified nucleic acid is carried out by reacting the sample with an oligonucleotide according to claim 8 under suitable hybridization conditions and detecting the presence of the label in any hybrids formed between the amplified sequence and the probe.

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11. Method according to claim 9, wherein the amplification technique used is a transcription based amplification technique and the first oligonucleotide is provided with a promoter sequence recognized by a DNA dependent RNA polymerase.

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12. Test kit for the detection of HIV-1 in a sample comprising:

- one or more oligonucleotides according any of claims 1-2,
- an oligonucleotide comprising a nucleic acid sequence substantially complementary to at least part of the amplified nucleic acid sequence , provided with a detectable label
- suitable amplification reagents.

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13. Test kit for the detection of HIV-1 in a sample comprising a pair of oligonucleotide according to claim 4, together with suitable amplification reagents and means for detecting the amplified nucleic acid.

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12Q 1/70	A1	(11) International Publication Number: WO 99/07898 (43) International Publication Date: 18 February 1999 (18.02.99)
(21) International Application Number: PCT/EP98/04945 (22) International Filing Date: 5 August 1998 (05.08.98) (30) Priority Data: 97202455.8 8 August 1997 (08.08.97) EP (71) Applicant (for all designated States except US): AKZO NOBEL N.V. [NL/NL]; Velperweg 76, NL-6824 BM Arnhem (NL). (72) Inventors; and (75) Inventors/Applicants (for US only): GOUDSMIT, Jaap [NL/NL]; Koninginneweg 4, NL-1075 CX Amsterdam (NL). OUDSHOORN, Pieter [NL/NL]; Wilgenstraat 6, NL-5271 JH St. Michielsgestel (NL). JURRIAANS, Suzanne [NL/NL]; Speet 33, NL-1141 BX Monnickendam (NL). LUKASHOV, Vladimir Vladimirovich [RU/NL]; Eeftink 621, NL-1103 AE Amsterdam (NL). (74) Agent: VAN GENT, M.; P.O. Box 20, NL-5340 BH Oss (NL).		(81) Designated States: AU, CA, ID, JP, KR, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN THE AMPLIFICATION AND DETECTION OF ALL SUBTYPES OF HIV-1		
(57) Abstract <p>The present invention is related to nucleic acid sequences that can be used in the field of virus diagnostics, more specifically the diagnosis of infections with the AIDS causing Human Immuno-deficiency Virus (HIV). With the present invention nucleotide sequences are provided that can be used as primers and probes in the amplification and detection of HIV-1 nucleic acid. The oligonucleotide sequences provided with the present invention are located in the LTR part of the HIV viral genome. It has been found that, by using the sequences of the present invention in methods for the amplification and detection of nucleic acid a sensitive and specific detection of HIV-1 can be obtained. The benefit of the sequences of the present invention primarily resides in the fact that, with the aid of primers and probes comprising the sequences according to the invention the nucleic acid of all presently known subtypes of HIV-1 can be detected with high accuracy and sensitivity. So far no primer pairs or hybridization probes have been developed that would allow the detection of such a broad range of HIV-1 variants. The oligonucleotide sequences according to the present invention are especially useful in methods for the amplification of nucleic acid.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/04945

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12Q1/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 617 132 A (GEN PROBE INC) 28 September 1994 see the whole document ---	1-13
X	US 5 629 413 A (PETERSON TODD C ET AL) 13 May 1997 see column 23 ---	1-3, 12, 13
X	EP 0 331 939 A (GREATBATCH GEN AID LTD) 13 September 1989 Y see esp. fig 11, ---	1-3, 12, 13 6
Y	EP 0 402 997 A (AKZO NV) 19 December 1990 see examples ---	6
A	WO 91 10746 A (CHIRON CORP) 25 July 1991 see the whole document -----	1-13

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

14 December 1998

Date of mailing of the international search report

21/12/1998

Name and mailing address of the ISA

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Authorized officer

Müller, F

INTERNATIONAL SEARCH REPORT

information on patent family members

Intel International Application No

PCT/EP 98/04945

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0617132 A	28-09-1994	AU 686616 B	12-02-1998
		AU 6551594 A	24-10-1994
		CA 2159103 A	13-10-1994
		JP 8508404 T	10-09-1996
		WO 9423069 A	13-10-1994
		US 5712385 A	27-01-1998
US 5629413 A	13-05-1997	AU 688364 B	12-03-1998
		AU 7551194 A	20-02-1995
		EP 0714436 A	05-06-1996
		JP 9501562 T	18-02-1997
		WO 9503407 A	02-02-1995
EP 0331939 A	13-09-1989	US 5580761 A	03-12-1996
		US 5324643 A	28-06-1994
EP 0402997 A	19-12-1990	AT 111533 T	15-09-1994
		AU 641399 B	23-09-1993
		AU 5716090 A	20-12-1990
		CA 2018877 A	15-12-1990
		DE 69012440 D	20-10-1994
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		DK 402997 T	31-10-1994
		ES 2063902 T	16-01-1995
		IE 64040 B	28-06-1995
		JP 3033656 A	13-02-1991
WO 9110746 A	25-07-1991	CA 2070632 A	11-07-1991
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		JP 5503422 T	10-06-1993
		PT 96458 A,B	31-10-1991
		US 5656731 A	12-08-1997
		US 5629153 A	13-05-1997

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference T/97300 WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 98/ 04945	International filing date (day/month/year) 05/08/1998	(Earliest) Priority Date (day/month/year) 08/08/1997
Applicant AKZO NOBEL N.V. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☒ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the **title**, ☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

Figure No. _____ ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/04945

A. CLASSIFICATION OF SUBJECT MATTER

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Date of the actual completion of the international search

14 December 1998

Date of mailing of the international search report

21/12/1998

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 98/04945

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0617132	A	28-09-1994	AU 686616 B	12-02-1998
			AU 6551594 A	24-10-1994
			CA 2159103 A	13-10-1994
			JP 8508404 T	10-09-1996
			WO 9423069 A	13-10-1994
			US 5712385 A	27-01-1998
US 5629413	A	13-05-1997	AU 688364 B	12-03-1998
			AU 7551194 A	20-02-1995
			EP 0714436 A	05-06-1996
			JP 9501562 T	18-02-1997
			WO 9503407 A	02-02-1995
EP 0331939	A	13-09-1989	US 5580761 A	03-12-1996
			US 5324643 A	28-06-1994
EP 0402997	A	19-12-1990	AT 111533 T	15-09-1994
			AU 641399 B	23-09-1993
			AU 5716090 A	20-12-1990
			CA 2018877 A	15-12-1990
			DE 69012440 D	20-10-1994
			DE 69012440 T	09-02-1995
			DK 402997 T	31-10-1994
			ES 2063902 T	16-01-1995
			IE 64040 B	28-06-1995
			JP 3033656 A	13-02-1991
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			EP 0510085 A	28-10-1992
			JP 5503422 T	10-06-1993
			PT 96458 A,B	31-10-1991
			US 5656731 A	12-08-1997
			US 5629153 A	13-05-1997